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ASPIRATED FOREIGN BODIES
SPECIAL REPORT

James Weaver, M.D.
Roy Klepser, M.D.

The purpose of this paper is to present an analysis of 30 cases of foreign bodies in the laryngo-tracheo-bronchial tree seen at Children's Hospital during the last 10 years, to review the mechanisms active and the physiopathologic effects in their presence, and to re-emphasize the principal points in diagnosis. Papers on this subject are "hardy perennials" in medical literature. However, since many cases presenting typical, or nearly typical, pictures of aspiration of a foreign body are still treated as bronchitis or pneumonia early in their course, it is not amiss to present them again for discussion.

The incidence of aspiration of foreign bodies is highest in children under 3 years of age. Clerf[1], in a series of 115 patients who had aspirated peanuts, found that 111, or 96%, were under 10 years of age, and that 48, or 67%, were under 3 years of age. In our series the oldest patient was aged 10 years, and the youngest aged 3 months, with an average age of 2 years and 3 months. Eighty per cent were less than 3 years old. The age incidence distribution is a resultant of several factors. Children in the younger age group are much more apt to place objects into the mouth, that being the first destination of anything given a small child, and the starting point for all aspirated foreign bodies. Maternal efforts at removal of foreign bodies from the mouth frequently cause a spasm of crying and gasping with accentuated inspiration, and resulting aspiration of the foreign material. Efficiency in mastication and deglutition of small objects, and materials which tend to fragment, is quite low in the younger age group. It is repetition of common knowledge to say here that young children should not be allowed contact with objects which may be placed entirely within the mouth, or which may necessitate swallowing in fragments, notably nuts.

Although no explanation can be advanced, it is interesting to note the race and sex incidence. Twenty-five cases were white, and 5 were colored. Eighteen were males, and 12 were females.

Foreign bodies may lodge at any point in the laryngo-tracheo-bronchial tree, this being dependent primarily on the size and contour of the object. The clinical picture varies considerably with the location.

Relatively large objects which are aspirated into the glottis may not pass the smaller aperture at the vocal cords. These cause very severe symptoms. The object may entirely block the airway, or may frequently impinge on the vocal cords, causing spasm and complete laryngeal obstruction.

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Cyanosis and death may result in these cases unless the foreign body can be removed immediately. Small sharp objects may also be aspirated only as far as the larynx. This results when a point or sharp corner of the object becomes imbedded in the lining mucosa.

Foreign bodies in the trachea are generally freely movable. The expiratory "slap" which is present in many cases of tracheal foreign body occurs when the foreign body hits against the trachea or larynx in its movements up and down with respiration.

Most objects which pass the larynx are of such size that they will enter and lodge in the bronchus. It is here that the great majority of air passage

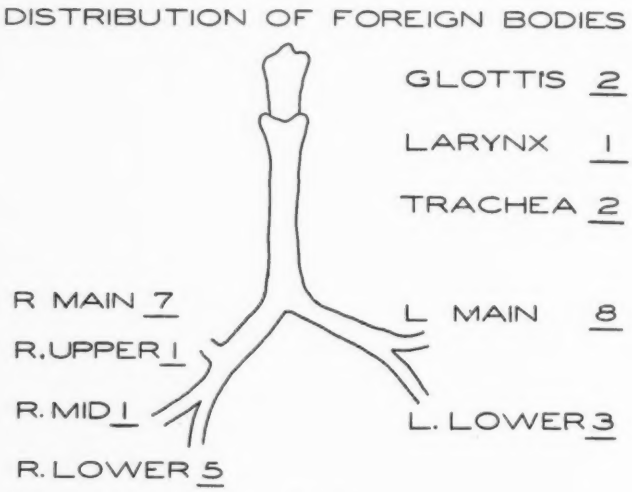

FIG. I

foreign bodies are found. One investigator[1] reported that of 413 cases of foreign bodies in the air passages, 337, or 82%, were in the bronchi. This is comparable to 25 of 30 cases, or 83%, in this series. Distribution of foreign bodies in the laryngo-tracheo-bronchial tree in this series is presented in Chart 1. These results conform in general to those expected. The right main stem bronchus comes off the trachea at a less acute angle than the left, so that it is easier for an object to find its way to the right side.

The diagnosis of foreign bodies in the air passages should be relatively easy in most cases. The prime prerequisite is consideration of aspiration as a causative factor in the case as it presents itself. This is most notably

true in patients who have complaints of sudden onset of respiratory difficulty, cough of obscure origin, and wheezing. The analysis of presenting complaints and symptomatology is in Chart 1.

CHART 1

Complaints and presenting symptoms

Sudden onset (26)	87%
Onset while eating (18)	57%
Cough (25)	83%
Wheezing (13)	44%
Fever (9)	30%
Cyanosis at onset (4)	13%
Dyspnea on exertion (3)	10%
Onset following anesthesia (1)	3%

This symptomatology gives some indication of the importance of a carefully taken history. In most cases the clue which leads to the correct diagnosis can be elicited with close questioning, and this clue is spontaneously given by the informant in approximately 90% of the cases. It is unfortunately true that in a small but important number of cases the initial incident of choking and gasping, followed by cough, and later fever, has been mentioned by the informant, only to be dismissed or forgotten by the physician. The correct diagnosis is therefore delayed.

Diagnosis may sometimes be obscured by lack of understanding of the mechanism of foreign bodies in the air passages, and failure to tie in clinical findings with resultant physical changes. Valve action has been used in many texts and papers to describe the mechanics of a foreign body in the bronchial tree. Such valve action may be divided into four types.

*1. The "by-pass" valve action is in effect when obstruction by the foreign body is incomplete in both inspiration and expiration. The bronchi dilate with inspiration, facilitating easy ingress of air. On expiration the bronchi contract, and the foreign object causes a relatively greater partial obstruction. This results in the "asthmatoid wheeze", first reported as a pathognomonic sign of foreign body by Jackson in 1919[2]. This type of obstruction early causes no change in the pulmonary tissue distal to the foreign body. Figure II illustrates the mechanism active.

*2. The "ball-valve" mechanism, with obstruction in expiration, is also dependent on the physiologic dilatation of the bronchi with inspiration, and contracture on expiration. In this type the air enters past the obstruction relatively freely, but on expiration the blockage becomes complete, and emphysema of the lung tissue distal to the obstruction rapidly results. The valve action is shown in Figure III.

*3. The "ball-valve" action, with obstruction in inspiration, occurs when the foreign body is more or less movable in the bronchus. On in-

spiration, with the bronchi dilated, the object slips distally further into the bronchial tube, completely blocking the entrance of air into the lung, and

FIG. II

FIG. III

on expiration it moves proximally into a tube of larger diameter, and thus allows egress of air. With diminution of air in the alveoli and bronchioles atelectasis results. Figure IV illustrates the valve action.

¾4. "Stop-Valve" action occurs when the object becomes so lodged in a bronchus that complete occlusion in both inspiration and expiration re-

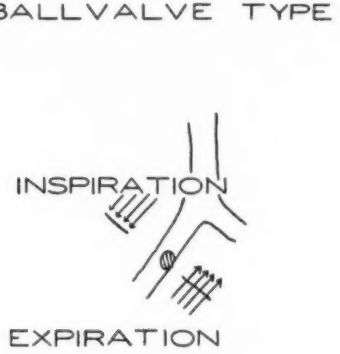

FIG. IV

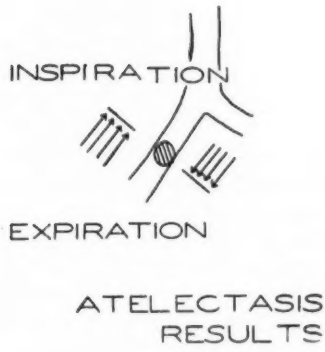

FIG. V

sult. In this state air distal to the obstruction is absorbed and atelectasis results. Figure V demonstrates the stop valve.

Results of physical examination of these patients not only vary in individual cases, but may vary from one time to another in the same case. Direct evidence of the presence of a foreign body, that is auditory slap and palpatory thud, are not so frequently encountered as indirect indications. Findings on examination which indicate atelectasis are the most common. Limitation of motion of the affected side of the chest is a very important but generally neglected, diagnostic sign. A summary of findings on examination in our cases is shown in Chart 2.

CHART 2

Physical findings in 30 cases of foreign body

Clinical signs of respiratory involvement (26)	87%
Atelectasis (15)	50%
Emphysema (3)	10%
Asthmatoid wheeze (14)	47%
Rales (9)	30%
Rhonci (5)	17%
Limitation of motion on one side (1)	3%
No signs of respiratory involvement (4)	14%

X-ray examination should be made of all patients in whom a respiratory foreign body is suspected. It is important to remember that a single frontal plane plate is not sufficient for accurate diagnosis. Lateral and oblique views, combined with fluoroscopic study, will often give very important information. Some foreign bodies, being radio-opaque, will be easily located and demonstrated by x-ray. This was true in 6 of the 22 cases in this series which were studied roentgenologically. In cases where the object cannot be demonstrated directly, the findings are dependent on changes from the normal x-ray due to obstruction of an air passage, or to an inflammatory process. Non-opaque foreign bodies which are functioning as by-pass valves will cause no radiographic changes until inflammation occurs. Atelectasis is the most common finding indicating the presence of a foreign body. This results when the object acts in the manner of an expiratory ball valve or as a stop valve. Emphysema of an obstructive nature results from inspiratory ball valve action. Compensatory emphysema may be found where the foreign body and atelectasis are present on the contralateral side. Shift of the mediastinum accompanies, to a variable degree, both atelectasis and emphysema. The mechanics or location of a foreign body in the air passages may frequently change. In view of this, physical examination at any one instant is more dependable evidence of the condition in the respiratory system than an x-ray taken some minutes or hours before. X-rays demonstrating some of the changes in cases of this series are shown in the accompanying figures.

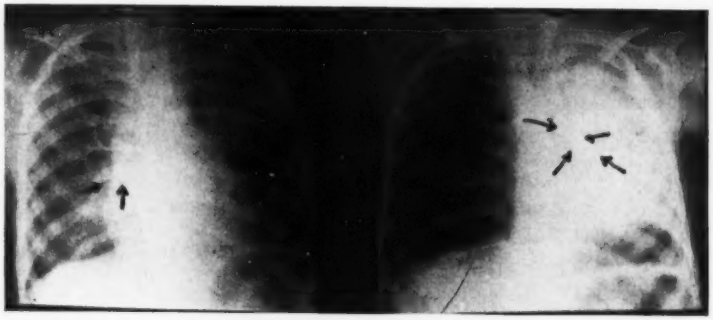

FIG. VI. Atelectasis and foreign body on the right, and the accompanying plate taken 4 hours later, showing the foreign body to have moved, and atelectasis to be present on the left.

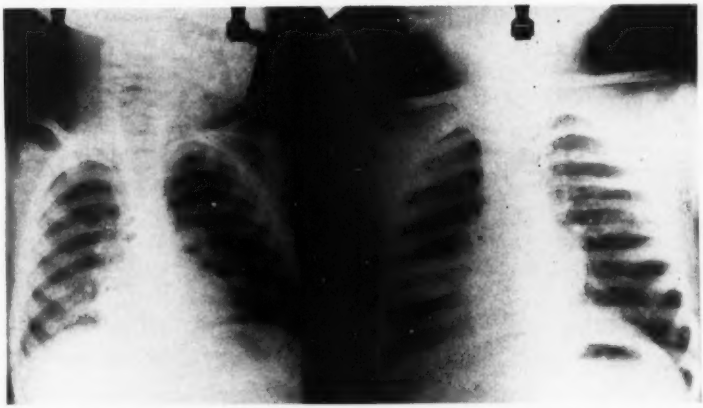

FIG. VII. Atelectasis of the right middle lobe due to a non-opaque foreign body in the middle lobe bronchus. The accompanying normal plate was taken after removal of the foreign body.

An analysis of roentgen findings is shown in Chart 3.

CHART 3

Roentgen findings in this series

The foreign body or evidence of its presence was detected in 78% of cases x-rayed.

Foreign body visualized	6
Evidence of foreign body	13
Atelectasis	6
Emphysema	2
Inflammation	5
No evidence of foreign body	6
No x-ray taken	5

Although x-rays are of great value in detection and diagnosis of foreign bodies in the air passages, they are by no means infallible. Cases in which the history and physical examination are suggestive should be treated as if a foreign body were present, in spite of negative x-ray findings.

FIG. VIII. Obstructive emphysema on the left prior to removal of the foreign body with bronchoscopy. The follow-up plate is shown.

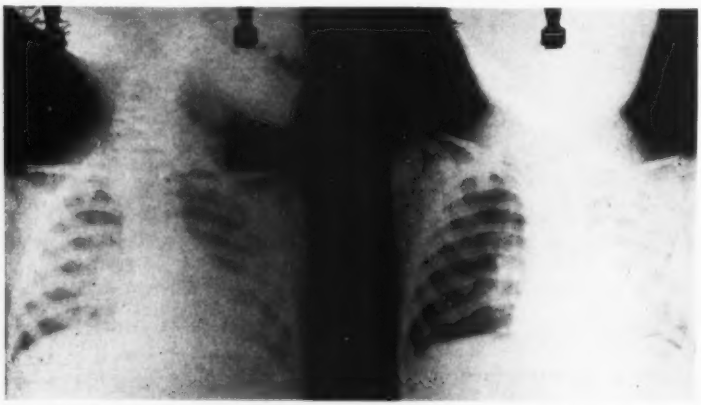

FIG. IX. Compensatory emphysema is demonstrable on the right. The foreign body was removed from the opposite side. Follow-up plate is shown.

Laryngoscopy and bronchoscopy are the basic measures in the treatment of foreign bodies in the air passages. Removal of the object as soon as possible should be the primary aim in all such cases. No discussion of foreign bodies would be complete without a reminder that endoscopy, and particularly bronchoscopy, will forever be indebted to Chevalier Jackson and his work in perfecting both technique and instruments in this field.

In this series of cases the foreign body was removed from the air passages in 26 of the 30 cases. One patient was referred to another hospital, in Philadelphia, after the object had been visualized bronchoscopically, but its removal found impossible. In two cases the foreign body was coughed up, one a gum drop in the glottis, and one a peanut in the bronchus. In 3 cases the foreign body was removed by direct laryngoscopy. Bronchoscopy was employed in 24 cases, removal being accomplished on the first attempt in 21 of these, and on the second try in 3. One case was not examined endoscopically. Additional therapy is, of course, necessary in some cases. This is especially true in cases where the foreign body has caused inflammation, or has resulted in an infectious process. The antibiotics are useful in the cases with infection, and adjunctive measures such as oxygen, steam inhalation, and postural drainage should be used as indicated.

The prognosis in the group of cases under discussion is good with prompt treatment. Adverse effects encountered are primarily dependent on the material present, and on the length of time that it has been in place. The vegetal foreign bodies, which predominate in this series as in most others, are the greatest troublemakers. They set up a local inflammatory reaction rapidly leading to tracheobronchitis, and later lung abscess. Metallic, and other more or less inert objects, tend to produce less inflammatory reaction. Any foreign object in the bronchial tree which remains there for any prolonged period will produce some reaction, and even though removed, may leave some bronchial stenosis. This condition may cause a subsequent and slowly developing bronchiectasis. Fifteen of the cases in this series showed moderate to marked bronchial inflammation when examined bronchoscopically. None have developed bronchiectasis as far as is known.

The foreign bodies and a summary analysis of their duration in the air passages are noted in Chart 4.

Immediate results in this series of patients were in general good. Nineteen patients had little or no difficulty after the foreign body was removed. Eight patients were acutely ill even after the aspirated object had been removed. Four of these exhibited a suppurative process in the lung, with probable early abscess formation. All eight cases responded to medical therapy, and were discharged as recovered. Two patients expired. One was a 21 months old white female who had aspirated a piece of timothy hay four weeks prior to admission. She was in poor condition on admission, ran a septic course in spite of bronchoscopic and thoracotomy drainage of the resultant lung abscess and supportive therapy, and expired on the 13th hospital day. Postmortem examination showed multiple lung abscesses in the right lower and middle lobes.

The second case ending fatally was an 18 month old white male who was admitted to the hospital with a diagnosis of pneumonia. He was a known asthmatic, and two weeks before had had an attack of asthmatic bronchitis

with fever. This was apparently clearing well until 2 days prior to admission when the patient became feverish and lethargic, and developed a respiratory grunt, and a severe persistent cough, productive of copious amounts of white phlegm. Examination revealed fever, asthmatic type of breathing, and signs of consolidation in the left chest. An x-ray taken the day following admission showed the left chest clear, and the right chest

CHART 4

Types of foreign bodies removed from air passages

Peanut fragments	13
Straight pins	2
Carrot fragment	1
Meat fragment	1
Chicken bone	1
Kernel of corn	1
Apple fragment	1
Timothy hay	1
Safety pin	1
Nut shell	1
Pecan	1
Crayon	1
Tooth	1
Button	1
Gum drop	1
Nail	1
Pebble	1

DURATION IN PLACE

Shortest	½ hour
Longest	3½ months
Average duration in place	15 days
Less than 24 hours	36%
Less than 5 days	60%

HOSPITALIZATION

Average hospital stay	6.6 days
Less than 5 days	75%

to have increased markings and infiltration, suggesting bronchopneumonia. Sulfadiazine and symptomatic therapy for asthma were given with some improvement, the temperature dropping to normal promptly, and remaining there. The asthmatic breathing continued with only slight improvement. On the 16th hospital day physical examination showed wheezing over the entire chest. No rales or signs of consolidation were detected. The next morning, the 17th hospital day, the patient developed severe inspiratory stridor, with deep epigastric and suprasternal retraction. The

chest was clear except for marked stridor. He was given an anti-spasmodic, and placed in a croup tent. Approximately 3 hours later the patient was found *in extremis*, and died shortly in spite of efforts at resuscitation.

Postmortem findings were rather unexpected. A half peanut, soft and covered with a whitish mucoid film, was found lodged in the lower trachea, at the carina. The mucous membrane in this area was edematous and reddened. In the wall of the right main bronchus near the bifurcation there was an area of mucosa, shaped like the peanut, which was red and swollen. It was thought that this may have been the initial site of lodgement of the foreign body. Lividity of the skin and congestion of the liver were the only other abnormal findings. The pathological diagnosis was "asphyxiation due to aspiration of a foreign body (peanut), and congestion of the liver."

The object lesson here is apparent but some points in the case should be mentioned. The asthmatic history was a great stumbling block in the way of diagnosis. A more carefully taken history may have revealed that the child had choked on peanuts at the onset of the illness. Physical signs of consolidation were found in the left chest on admission, but an x-ray taken 24 hours later showed the left chest clear and the right chest to have infiltration and increased markings. This change in conditions probably occurred when the foreign body shifted position during a coughing episode, and should, perhaps, have aroused more comment and investigation. The final indication of mistaken diagnosis was the sudden change from expiratory difficulty and wheeze to severe inspiratory difficulty and stridor.

It is impossible to give a long range prognosis in this series of cases. To date none of these patients have been readmitted to this hospital with either bronchiectasis or lung abscess.

SUMMARY

We have presented a series of 30 proven cases of foreign body in the laryngo-tracheo-bronchial tree. This is the total number of such cases which could be found in the records at Children's Hospital for the last 10 years. Pertinent information concerning these cases is recorded, and an outline of some of the clinical aspects of this condition is included. Sixteen of the 30 cases were seen within the last 2 years, i.e. 1946 and 1947. This could indicate a laudable increase in frequency of diagnosis by the physician.

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UNUSUAL RETROPHARYNGEAL ABSCESS COMPLICATED BY ERYTHEMA NODOSUM

Case Report No. 126

Harry Robelen, M.D. S. R. 46-2411

S. R., a 6 year old white male, was well until June 17, 1947 when he complained for the first time of a sore throat and a slight fever was noted. The next day there was a headache and the fever persisted. On the third day he developed a fever of 103° and a fullness was noticed beneath the angle of both jaws. He was admitted to Children's Hospital on June 20, 1947.

The family history was non-contributory. The past history revealed that he was the result of an 8 month pregnancy terminated by Caesarian section because of a previous placenta previa. The birth weight was 7 lbs. 2 oz. He had had measles, chicken pox and infrequent colds. There had been a tonsillectomy and adenoidectomy in 1946.

Physical examination at this time revealed a well developed, well nourished white male appearing acutely ill. His temperature was 104.2°. The left posterior pillar was edematous and inflamed with small white areas of exudate. The pillar was pushed forward and medially. There was no fluctuation. There was marked swelling of the left upper lateral neck which was very tender. The cervical glands were enlarged and tender and there was some stiffness of the neck. Respiratory excursions were normal. The impression was that the patient had a beginning abscess posterior to the left tonsillar fossa.

Laboratory work on admission revealed a hemoglobin of 10 gms. with 3.9 million red blood cells, 24,600 white blood cells with 92% polys. Urinalysis was negative.

Treatment on admission consisted of penicillin, 30,000 units every 3 hours, and sulfadiazine, grains 7.7 every 4 hours day and night.

In five days the temperature dropped to normal and with the exception of a spike to 102.6° on the sixth hospital day, it remained below 100.2° until the 25th day. The acute infection seemed to subside rapidly under medication. The swelling in the throat showed definite improvement by the second day, and the cervical glands decreased in size. On June 26, 1947 the sulfadiazine was discontinued. The patient's general condition was good and he felt well with the exception of continued stiffness of the neck.

On June 30, 1947 x-ray of the cervical spine showed considerable soft tissue swelling extending the whole course of the retropharyngeal and retrolaryngeal spaces probably representing an acute inflammatory process

(Figure 1). Clinically, the condition was thought to be subsiding. There was no area of fluctuation in the throat. On July 12, 1947 the anterior cervical glands which had subsided appeared to be enlarging again and

FIG. I: S.R. Lateral cervical view showing the marked increase in the spaces between the anterior border of the vertebral bodies and the posterior border of the trachea.

the sulfadiazine and penicillin were started again. A two hundred cc. transfusion of whole blood was given.

On July 14, 1947 incision and drainage of the retropharyngeal mass was attempted but no pus was obtained. Following this, the temperature

spiked to 102° and continued to rise daily. On July 16th the sulfadiazine was stopped because of mild hematuria.

On July 17, 1947 streptomycin, 125,000 units every 3 hours, was begun. Penicillin was increased to 100,000 units every 3 hours. On July 18, 1947 maculo-papular and nodular lesions appeared on the extremities. The nodules were tender to touch and were thought to represent bacterial metastases.

On July 19, 1947, the 30th hospital day, another operative attempt through the mouth produced putty-like pus from an incision lower than the first. Culture showed a growth of non-hemolytic streptococci sensitive to 0.125 units of penicillin per cc. Three hundred cc. of whole blood was given. The streptomycin was discontinued overnight. The next day the skin lesions appeared more active and larger, some coalescing. The temperature continued to rise and the patient appeared acutely ill. Streptomycin was started again and sulfathiazole therapy was instituted at this time.

On July 21, 1947 the penicillin dosage was increased to 200,000 units every 3 hours. The temperature spiked to 104°. The patient seemed quite ill with considerable discomfort from painful skin lesions. The following day he was somewhat improved, sitting up in bed playing and feeling rather well between periods of fever. The skin lesions appeared to be subsiding and presented fading centers with surrounding erythema. The centers were indurated and slightly tender. The rash now appeared allergic in nature.

The next day 300 cc. of whole blood was given. The fever was still spiking as high as 103° daily. On July 24, 1947 the streptomycin was discontinued. X-ray of the long bones at this time was reported as negative for any osteal or periosteal changes. The temperature subsided overnight from 102–103° to normal. On July 25, 1947 the skin lesions were definitely less angry appearing. Sulfathiazole was discontinued. An x-ray on July 26 showed a decrease in the size of the retropharyngeal swelling. The temperature remained normal. Laboratory work-up at this time showed a hemoglobin of 13 gms. with 4.1 million red blood cells, 17,000 white blood cells with 73% polys. The next day the white-cell count was 10,000. Penicillin was discontinued on the 28th of July.

Following the cessation of the streptomycin, the rash subsided rapidly. Examination on the 30th of July revealed fairly complete extensibility of the neck for the first time. There was no lymph node enlargement. The skin still showed some pigmentation at the site of the lesions. The patient was discharged in good condition and has remained so during his follow-up dispensary visits.

DISCUSSION

John A. Washington, M.D.: Ten days after penicillin and sulfadiazine therapy was started the patient seemed cured except for one finding which was stiffness of the neck. Extension was markedly limited and rotation in both directions was moderately limited. Looking into the throat, one was not conscious of fullness of the posterior wall. Tonsillar swelling had subsided and cervical adenitis had about disappeared. The boy was lively and was eating well. A lateral x-ray of the neck showed conspicuous swelling anterior to the cervical spine, presumably due to retropharyngeal and retrolaryngeal inflammation.

Two more weeks of penicillin therapy produced no diminution of the swelling as seen by x-ray. Worse than this, the anterior cervical lymph glands were beginning to swell again suggesting that the infecting organism was developing penicillin resistance. At this point the first incision of the posterior pharyngeal wall was made. Pus was not found. The day following, fever commenced for the first time since the week of admission. It seemed that the infection was getting more and more out of hand. Penicillin dosage was increased and in addition streptomycin was begun on the chance that it might help.

The day following the start of streptomycin additional concern was caused by the appearance on the arms and legs of discrete maculo-papular and nodular skin lesions. The nodules were very tender to touch and appeared to be bacterial metastases; it was thought probably due to staphylococci. A further attempt to drain the mass in the neck seemed obligatory and through a second incision, cheesey pus was evacuated. Streptomycin and sulfadiazine were discontinued overnight. The following day the cervical adenitis was reduced but the nodules in the skin had enlarged and in places coalesced. They were very painful. The boy looked seriously ill for the first time and the temperature rose rapidly. Streptomycin and sulfadiazine were started again on the assumption that bacterial metastases were spreading.

Four days after the appearance of the skin lesions, the nodules began to flatten out and developed pale centers of clearing erythema. None became fluctuant and the lesions took on the appearance of allergic manifestations rather than abscesses. Blood cultures remained sterile.

On the sixth day of the rash streptomycin was stopped following which the rash and fever subsided so rapidly that a definite connection seemed to have existed. Sulfathiazole was discontinued a day later and penicillin three days later. X-ray showed resolution of the retropharyngeal mass.

The nature of the skin lesions remains undetermined. Their occurrence at a time when the infection was becoming active in spite of the use of

penicillin made the initial diagnosis of bacterial metastases quite tenable. If this was correct, the strenuous use of antibiotics may have prevented suppuration and so modified the lesions that in their subsiding stage they appeared allergic in nature. Points against regarding them as bacterial are that they occurred only on the extremities, blood culture was sterile, and the retropharyngeal abscess was due to a streptococcus while the fresh lesions were the type seen in staphylococcal septicemia.

If non-bacterial, as seems probable, the term erythema nodosum must be applied to the lesions. It is possible that allergy to the streptococcus in the retropharyngeal abscess was responsible. A more likely cause would be a cutaneous sensitivity to sulfadiazine. This drug was administered during the week after admission and again during the ten days preceding the appearance of the rash. It was discontinued the day before the rash appeared. Sulfathiazole was given after the rash appeared and was continued until after the nodules subsided. Finally one cannot disregard the fact that streptomycin was started on the day before the rash appeared and that although the lesions were undergoing some resolution before the drug was stopped, there was striking subsidence the day after the drug was withdrawn with a corresponding drop to normal of the temperature. For reference it seems proper to record the case under a heading which will draw attention to this coincidence.

OIL OF WINTERGREEN POISONING

Edwin B. Vaden, M.D.

D. L. 48-3692
J. R. 44-6479

Oil of wintergreen (methyl salicylate) poisoning is not an uncommon occurrence, and it is of particular importance in the practice of pediatrics because the majority of cases have occurred in infants and children following the accidental ingestion of methyl salicylate. There is a high mortality (59 per cent in Stevenson's[1] series of 46 patients) and in several instances fatalities have occurred in infants following the ingestion of only 4 cc. of oil of wintergreen. At Children's Hospital there have been 2 cases of oil of wintergreen poisoning in the past two and one-half years.

Case No. 1: D. L., an eighteen-month old colored male, was admitted to Children's Hospital on March 31, 1948 because of rapid breathing and vomiting with a history of ingestion of an unknown amount of methyl salicylate ten hours prior to admission. The mother had found the infant choking and crying with an empty one-ounce bottle of oil of wintergreen on the floor beside him and with some of the liniment spilled on the rug. A young sister had been playing with the bottle and had left it within reach of the patient. He was given a drink of water and vomited immediately, then became irritable and drowsy. The mother was advised by her physician to give him large quantities of water to drink, and although he was very thirsty, he vomited each time following ingestion of the water. His irritability increased and he began breathing deeply about 7 hours after swallowing the medication. He was then taken to his local physician who referred him to this hospital, where he was admitted to the ward 10 hours after the ingestion of the methyl salicylate.

Birth and developmental histories were normal and the family history non-contributory.

The admission physical examination revealed a well-developed and well-nourished colored male, weighing 26 pounds, whose breathing was deep and rapid (58 per minute). He was very pale and irritable. The pulse rate was 132 per minute, and the rectal temperature was 99.2° F. The pharynx was mildly injected. There were no other positive physical findings.

Laboratory studies on admission revealed a carbon dioxide combining power of 20 volumes per cent. Urinalysis was positive for acetone. A hemogram revealed 11 grams of hemoglobin and the white cell count was 15,000 with 72% neutrophils, 26% lymphocytes and 2% monocytes.

During the night following admission he received an intravenous infusion of 250 cc. 5 per cent glucose in Hartmann's solution, followed by 240 cc. M/6

sodium lactate by vein and a second 240 cc. M/6 sodium lactate by hypodermoclysis; in addition, he took water and a saline orange juice-glucose solution by mouth. However, in the morning, 10 hours later, the patient appeared more irritable and there was no improvement in the hyperpnea; the carbon-dioxide combining power had dropped to 13 volumes per cent and the blood pH was 7.25. At this time a continuous intravenous was begun and during the next 48 hours, the patient received large quantities of M/6 sodium lactate, 5 per cent glucose in normal saline and 2 whole blood transfusions. The patient was worse twenty-four hours after admission, at which time he was in a semi-stuporous condition. However, the carbon-dioxide combining power rose to 50 volumes per cent on the third day, and there was rather marked clinical improvement. Penicillin therapy was begun on the third day because of the appearance of rales in the chest and x-ray evidence of a pneumonic infiltration. The temperature rose to 103° F. (rectally). On the fourth day the carbon-dioxide combining power was 46 volumes per cent and the blood pH was 7.4. He showed marked improvement and began taking fluids and food by mouth. The remainder of his hospital course was uneventful.

He was discharged on the 13th hospital day, at which time the laboratory studies were normal and the patient asymptomatic.

Case No. 2: J. R., a twenty-one month old colored male, was admitted to Children's Hospital on October 10, 1945 with a history of having drunk approximately 10 cc. of "wintergreen liniment" 20 hours before admission. It was stated that he "cried violently" immediately after swallowing the drug, and that upon being given a drink of milk, he vomited promptly. He continued to vomit throughout the day and night and spent a very restless night. He was said to be crying upon awakening, and at this time, the parents stated that he was "limp and his eyes were rolled back."

The admission physical examination revealed a well-developed, well-nourished colored male infant with very rapid and shallow respirations and in a semi-comatose state. His temperature was 102.2° F. rectally. The only other physical finding noted was the presence of bilateral, moist, bubbling rales over both lung fields.

The patient had a convulsion while being examined on the ward and expired shortly afterward. There had been insufficient time to obtain any laboratory work or institute therapy.

An autopsy was performed by the coroner, but microscopic sections were not obtained by our laboratory. Grossly the abnormal findings were slightly dilated right auricle and ventricle, intensely congested and edematous lungs, congestion of the liver and kidneys and generalized lymphoid hyperplasia.

DISCUSSION

The two cases reported above show the well-recognized clinical picture of salicylism. There is early vomiting, extreme thirst, rapid and deep respiration, rapid pulse, cyanosis, and followed in the fatal cases by stupor, coma, impaired vision and hearing and convulsions with death due to respiratory and cardiac failure. The usual positive laboratory findings are a low carbon-dioxide combining power, a decrease in blood pH, a prolonged prothrombin time and a slightly increased or normal blood sugar. The urine is markedly positive for acetone and the Gerhart test for salicylates is positive. Frequently albuminuria is present and less frequently granular casts or red blood cells are present in the urine.

The pathological changes occurring in salicylate poison are extensive, and the pathological picture is fairly constant. The most outstanding finding is the presence of petechial hemorrhages in the serous membranes and generalized congestion of the organs. Hemorrhages have been found constantly in the pleura, pericardium, omentum, mesentery, the glia and the meninges. Some authors have reported the presence of hemorrhages in the stomach, brain, lungs, myocardium and in the mucosa of the stomach. There is frequently reported a fatty degeneration of the kidneys and of the liver.

That salicylate intoxication can produce many of the symptoms exhibited by these two cases, and a fairly well-defined postmortem picture is well-recognized, but there is a considerable divergence of opinion as to the mechanisms underlying the various physiological and pathological-anatomical changes. The mechanism of the poisoning is considered to be identical in acetyl salicylic acid, sodium salicylate and methyl salicylate intoxication but the greater toxicity of the latter is attributed to its relative retention in the body. Stevenson[1] states that ingested sodium salicylate is 80 per cent recoverable in the urine, and its excretion is completed in a period of 3 days, whereas methyl salicylate is 51 per cent recoverable in the urine as the acetyl salicylic, and its excretion requires 4 days.

The initial vomiting is due to the direct gastric irritation by the drug, although central nervous system stimulation may contribute to the vomiting.

Johnson[2] attributed the hyperpnea to an acidosis resulting from the accumulation of lactic acid and other fixed acids. Other workers (Odin[3], Barnett and associates[4] and Dodd and her group[5]) have demonstrated that the hyperpnea may supervene when the blood and urine pH are normal, a fact which suggests primary stimulation of the respiratory center. The first two studies suggest that the salicyl radical directly affects the respiratory center. Dodd and her associates concluded from

animal experiments thta changes in body temperature, the sensation of heat and the increase in gaseous metabolism induced by the salicylates are more important factors than central stimulation in the production of the hyperventilation.

Erganian and associates[6] in 1947 reported 13 cases of salicylate intoxication, 11 due to large doses of aspirin or "cold" medicine and 2 cases due to accidental ingestion of methyl salicylate liniment. This group explains the sequence of events by ascribing the initial hyperventilation to the direct stimulation on the respiratory center, which leads to an uncompensated respiratory alkalosis with compensation brought about rapidly by the kidneys with excretion of the excess bicarbonate resulting in an alkaline urine initially. The development of a ketosis plus the depleted sodium bicarbonate next brings the shift toward a metabolic acidosis, making it imperative for the hyperventilation to continue so that there will not be a relative excess of carbonic acid. At this point the hyperventilation is a physiological necessity and not merely a manifestation of salicylism; the respiratory center may have undergone poisoning and the patient may no longer be able to keep apace of the metabolic demands and if either of these factors is present, then metabolic acidosis may ensue.

In regard to the effect of the protracted vomiting on the acid-base balance, there is also a difference of opinion. Theoretically a loss of hydrochloric acid due to vomiting would produce an alkalosis; actually in children, vomiting is more often associated with an acidosis which, in severe cases, (characterized by an intense air hunger, rapid pulse, dehydration and stupor) resemble that found in advanced diabetes.

The prothrombin deficiency which is found following the administration of salicylates was first demonstrated in rats by Link[7] and his associates, whose studies on dicumeral, the active agent producing the hemorrhage in sweet clover disease, suggested that the compound was broken down into salicylic acid in the body. These workers succeeded in producing a hypoprothrombinemia in rats by feeding salicylates to the animals with a vitamin K deficit and produced in some instances hemorrhagic manifestations identical to those found in sweet clover disease. The mechanism producing the hypoprothrombinemia is obscure, but Govan[8] postulates that it is the result of liver damage rather than of a direct action on the circulating prothrombin. It is correctible by the administration of vitamin K.

The hemorrhagic findings at most are probably due in part to the prothrombin deficiency, but as has been pointed out by Link[7], prothrombin deficiency alone cannot be responsible for the hemorrhages. It is likely that vascular trauma and dilation, plus the prothrombin deficiency produce the bleeding.

The therapy consists of elimination of the source of the poison by gastric lavage when seen early. Most writers have suggested the use of sodium bicarbonate solution in lavaging and the introduction of sodium bicarbonate in the stomach, but Williams and Panting[9] stress the point that sodium bicarbonate should not be used, since in the early stage of acute salicylism it may actually increase the salicylate absorption.

To treat the alkali deficit, the use of M/6 sodium r-lactate in Ringer's solution is considered the safest and most efficacious of the alkalies. Barnett et al.[4] believe that it is most readily metabolized in the presence of salicylate intoxication, and it has the advantage of being both safer and easier to give than sodium bicarbonate solution.

Various investigators have demonstrated that a deficiency of glycogen and thiamine are likely factors in predisposing to sensitivity to salicylates, and in children, acute or chronic illness with anorexia or vomiting leads to depletion of the glycogen reserve and to vitamin deficiency. The use of large amounts of 10 per cent dextrose solution in conjunction with the M/6 sodium lactate solution tends to restore the glycogen reserve, as well as to further correct the dehydration. The correction of the thiamine deficiency by the administration of thiamine hydrochloride will theoretically reduce the sensitivity to salicylates.

The hypoprothrombinemia is correctible by the administration of vitamin K. The use of vitamin C is indicated, especially in view of the vascular changes found at autopsy. Ritz and associates[10] showed a low vitamin C content in animal tissue as one of the toxic manifestations of salicylism. The hemorrhagic tendencies are further combatted by repeated small whole blood transfusions.

In contrast to diabetic acidosis and its dramatic response to alkaline therapy, there is a very slow recovery in correction of acidosis due to salicylates even when the carbon-dioxide combining power has returned to normal, probably due to the fact that there is a continued respiratory stimulation, as several days are required for the elimination of the drug.

SUMMARY

Two cases of methyl salicylate intoxication (one fatal) occurring at Children's Hospital have been presented. The typical clinical picture and the post mortem findings have been described and the mechanism producing the physiological and pathological changes discussed.

The high mortality rate in methyl salicylate poisoning can be reduced by the recognition on the part of the laity and medical profession of the extreme toxicity of this drug and by the immediate and energetic treatment of methyl salicylate intoxication.

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CLINICO-PATHOLOGICAL CONFERENCE

Directed by: E. Clarence Rice, M.D.
Assisted by: Adrian Recinos, Jr., M.D.
Howard S. Madigan, M.D.
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By Invitation: David L. Weinstein, M.D.

Adrian Recinos, M.D.

J. M., a colored female, aged 22 months, was referred to Children's Hospital August 9th as a possible case of poliomyelitis. She had been well until two weeks before admission when she developed anorexia and listlessness followed by intermittent fever and occasional vomiting. These symptoms persisted and finally the child became very weak and could walk only with difficulty. She was then taken to a physician and referred to this hospital.

Past history revealed a normal birth, nutrition and development. There was no history of immunizations, contagious diseases, accidents or operations. At the age of four months the patient was hospitalized for bloody diarrhea. She had been exposed on a few occasions to a neighbor with pulmonary tuberculosis.

Family history disclosed no known familial diseases; however, the mother was "treated for the blood" during the last three months of pregnancy and continued treatment irregularly after delivery.

Physical examination on admission revealed a drowsy and listless colored child who responded only to painful stimuli. The temperature was 99°F. The skin and mucous membranes were warm and dry. The anterior fontanel was flat and measured 1.5 cm. in diameter. The sutures were slightly separated. The discs showed early papilledema with congestion of the retinal veins. There was paresis of the left abducens nerve and questionable facial weakness. The neck was moderately rigid. The left lower extremity was flaccid and the right slightly spastic. The deep reflexes were markedly hyperactive but equal, and the Babinski was positive bilaterally. The heart and lungs were normal. The liver and spleen were not palpable.

Lumbar puncture was productive of markedly xanthochromic fluid under no increased pressure and affected only slightly by jugular compression. The fluid contained one leucocyte per cubic millimeter, normal sugar content, and 2,000 mg. per cent protein. An x-ray of the skull was normal; 0.1 mgm. OT was negative and the Schick test was positive. Urinalysis was normal.

A subdural hematoma was suspected and trephine openings were made in both parietal regions of the skull the day after admission. The dura on the left was thickened in comparison to the right but no hematoma was found. Eighty-five cc. of clear fluid was removed from the ventricles and replaced by air. X ray examination revealed all portions of the ventricular system to be markedly dilated. The fluid contained 50 leucocytes per cu. mm. (90 per cent polymorphonuclears), normal sugar content, and 30 mg. per cent protein. The culture was sterile.

During the next few days the patient's condition remained essentially the same except that the temperature rose gradually and fluctuated between 102 and 104° F. X-ray of the chest on the third hospital day revealed an inflammatory lesion extending from the second to the fourth inter anteriorly in the inner right lung field suggestive of an early pneumonia. The patient was found dead in bed on the tenth hospital day.

DISCUSSION

David L. Weinstein, M.D.: A brief summary of the case gives us a picture of fatal illness of three and one half weeks duration. The onset is certainly not typical of any specific illness; however, the fact that two weeks had elapsed before hospitalization, during which time the infant was apparently following a down-hill course, leads one to feel that a critical situation is at hand.

This is borne out by the physical findings and an x-ray examination, where we find three major features:

1. Evidence of increased intra-cranial pressure.
   a. Slight separation of the sutures
   b. Paresis of the 6th and 7th nerves
   c. Ventricular dilatation
   d. Papilledema
2. Xanthochromic fluid.
3. Inflammatory lesion in the right lung field.

Increase of intra-cranial pressure may be due to any irritation or infection of the meninges. Xanthochromic fluid points to hemorrhage into the cerebrospinal fluid of relatively long standing, or it might signify fluid stasis.

This case represents a combination of these two factors with the rather unusual phenomenon, the clear ventricular fluid but markedly xanthochromic spinal fluid with a protein content almost a hundred times the normal. This feature closely resembles a Froin syndrome which is often found in cord tumors. It seems, then, that we are dealing here with a sub-tentorial condition, either inflammatory, hemorrhagic or neoplastic in origin.

Tuberculous meningitis must be considered first on the basis of tuberculosis contact and an inflammatory lesion of the chest. However, normal sugar content, negative tuberculin test, absence of evidence of miliary tuberculosis, choroidal tubercle, etc., discounts that diagnosis.

Tuberculoma without meningitis is possible and cannot be ruled out. Brain abscess without middle ear infection or other suppurative focus would be very rare. Lethargic encephalitis, poliomyelitis, acute infectious meningitides from staphylococcus, streptococcus, pneumococcus, etc., may be eliminated from consideration on the basis of physical examination and laboratory findings.

Chronic lead poisoning should be mentioned, although there is nothing in the history to suggest such a diagnosis, and we have no data in the case report relative to an investigation of this possibility.

Syphilitic involvement of the central nervous system must be considered. Here, also, we are given no x-ray or laboratory data upon which to base such a diagnosis. Toxoplasmosis is a remote possibility but one would expect more pulmonary and encephalitic phenomena.

An organized subdural clot, with or without secondary infection, exerting pressure on the lower region of the brain stem, could readily be the major etiological factor here; but there has been no rapid enlargement of the head, no history of trauma, no convulsions, and parietal trephination was negative. X-ray showed uniform dilatation of the ventricles and no evidence of cerebral hemisphere displacement. This would not be likely in the case of a subdural hematoma.

Subarachnoid hemorrhage would have resulted in a more acute illness with evidence of blood in the ventricles and spinal fluid.

Neoplasm in the region of the cerebellum or neuro-axis cannot be eliminated from consideration. Subtentorial tumors are twice as common as those above the tentorium. The duration seems rather short for neoplastic disease. However, the history is very often inadequate and parents are frequently not cognizant of symptoms.

I think that the inflammatory process in the right lung was probably a terminal affair. It could, however, readily be interpreted as a tuberculous process or a metastatic tumor.

On the basis of past experience at Children's and Gallinger Hospitals, I would diagnose this case as tuberculous meningitis, despite the negative tuberculin test. A negative tuberculin test would not be unusual in the face of an overwhelming infection. On the other hand I cannot associate a normal sugar content with tuberculous meningitis. Tuberculoma without meningitis cannot be ruled out.

An evaluation of all factors, however, leads me to the conclusion that we are dealing here with an intracranial tumor, probably originating in the

cerebellum, extending down the cord, and causing obstruction to the circulation of the cerebrospinal fluid. The suggestive Froin syndrome also points strongly to the diagnosis of subtentorial tumor.

John Cassidy, M.D.: Despite the absence of a history of trauma, the first impression as to diagnosis was that this patient had a subdural hematoma, based on the neurological findings and on the presence of marked xanthochromia of the spinal fluid, a marked increase in its protein, normal sugar content, and cell count.

After the trephining of the skull and the discovery of an internal hydrocephalus with no hematoma being found, the diagnosis of tuberculous meningitis was considered. The basis for this was the history of exposure to an active case of pulmonary tuberculosis, the demonstration of a suspicious pulmonary lesion by x-ray, and the presence of an internal hydrocephalus. It is not infrequent to find an obstruction to the circulation of cerebro-spinal fluid in cases of tuberculous meningitis and consequent dilatation of the ventricles due to the thick, fibrino-purulent gelatinous exudate which is usually present over the base of the brain.

One point for consideration is the labeling of a negative reaction to 0.1 mgm. of old tuberculin as a negative tuberculin test. It is negative for that amount of tuberculin but an individual should not be considered a non-reactor to tuberculin until the second strength PPD has been given.

The autopsy findings bore out the clinical impression. There was miliary tuberculosis involving the lungs, pleura, spleen, liver and kidneys. The convolutions of the cerebral hemispheres were considerably flattened due to the dilatation of the ventricles, and there were many small yellowish-grey tubercles scattered about. Over the base of the brain there was a dense yellowish-green fibrino-purulent exudate which extended around the brain stem and between the right and left cerebellar hemispheres. On sectioning the brain many tubercles were found in the ependyma and choroid plexus.

E. Clarence Rice, M.D.: It is difficult to reconcile the spinal fluid findings with the known pathology; however, it is well to remember that the laboratory examinations may occasionally give results which are not what one would expect in tuberculosis of the meninges. At times we have seen low and even normal spinal fluid cell counts. The spinal fluid sugar which is usually quite low or absent was reported to be quite normal in this case. Possibly the hemorrhage may have served to elevate the sugar content. In tuberculous meningitis the sugar content of the cisternal fluid will be found to be higher than that from the lumbar regions. It is well to remember also that this condition is one of the commonest causes of bloody or xanthochromic spinal fluid in children two years of age or under due to the erosion of the blood vessels of the brain and meninges by the tubercles.